Nebraska Department of Health and Human Services

HEALTH ALERT NETWORK

Advisory

TO: Nebraska Healthcare Providers

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RE: FDA Drug Safety Communication: Codeine use in certain children after tonsillectomy and/or adenoidectomy may lead to rare, but life-threatening adverse events or death

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Information for Health Care Professionals

- Life-threatening adverse events and death have occurred in certain children who received codeine after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. These children had evidence of being "ultra-rapid metabolizers" of substrates of cytochrome P450 2D6 (CYP2D6), including codeine. Some people have DNA variations that make this enzyme more active, causing codeine to be converted to morphine in the liver faster and more completely than in other people.
- Estimated numbers of ultra-rapid metabolizers vary among different racial/ethnic groups with substantially higher prevalence demonstrated among Ethiopian populations (29% vs. only 6.5% [for African American and Caucasion populations]).
- These "ultra-rapid metabolizers" are more likely to have higher than normal amounts of morphine in their blood after taking codeine which can result in breathing difficulty, which may be fatal.
- Taking codeine after tonsillectomy and/or adenoidectomy may increase such risk for breathing problems and death in children who are "ultra-rapid metabolizers."
- FDA-cleared tests are available for determining a patient's CYP2D6 genotype.
- If prescribing codeine-containing drugs, use the lowest effective dose for the shortest period of time on an as-needed basis (i.e., not scheduled around the clock).
- Counsel parents and caregivers on how to recognize the signs of morphine toxicity, and advise them to stop giving the child codeine and to seek medical attention immediately if their child is exhibiting these signs.
- Consider prescribing alternative analgesics for children undergoing tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome.
- Report adverse events involving codeine to the FDA MedWatch program. Either call 1-800-FDA-1088 to report by telephone or complete voluntary reporting Form FDA 3500 available at http://www.fda.gov/Safety/MedWatch/HowToReport.

The U.S. Food and Drug Administration (FDA) is reviewing reports of children who developed serious adverse effects or died after taking codeine for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. Recently, three pediatric deaths and one non-fatal but life-threatening case of respiratory depression were documented in the medical literature. These children (aged two to five years) had evidence of an inherited (genetic) ability to convert codeine into life-threatening or fatal amounts of morphine in the body. All children had received doses of codeine that were within the typical dose range.

FDA is currently conducting a safety review of codeine to determine if there are additional cases of inadvertent overdose or death in children taking codeine, and if these adverse events occur during treatment of other kinds of pain, such as post-operative pain following other types of surgery or procedures. FDA will update the public when more information is available.

Parents and caregivers of children taking codeine should be advised to observe for unusual sleepiness, confusion, or difficult or noisy breathing in their child and to stop giving their child codeine and seek medical attention immediately if such signs of overdose are present.

Additional Information to Provide to Parents and Caregivers of Children Given Codeine

- Certain children may be at risk for life-threatening side effects, such as breathing difficulty, or death when taking codeine for pain relief after tonsillectomy or adenoidectomy. This can occur even with use of codeine at recommended doses.
- Codeine is usually prescribed on an "AS NEEDED" basis. Do not administer codeine to the child on a regular basis UNLESS the child requires the drug. Do not administer more than six (6) doses per day.
- Signs of serious side effects of codeine in children can include unusual sleepiness, confusion, and difficult or noisy breathing. **If your child shows these signs, stop giving your child codeine and seek medical attention immediately by taking your child to the emergency room or calling 911.**
- Talk to your child's health care professional if you have any questions or concerns about codeine.
- Report adverse events involving codeine to the FDA MedWatch program. Either call 1-800-FDA-1088 to report by telephone or complete voluntary reporting Form FDA 3500 available at http://www.fda.gov/Safety/MedWatch/HowToReport.

Data Summary and Further Information Available From FDA Here:

http://www.fda.gov/Drugs/DrugSafety/ucm313631.htm#data